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PATENT

_	COOPERATION TREATY	~~
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PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Assistant Commissioner for Patents United States Patent and Trademark Office

From the INTERNATIONAL BUREAU

Box PCT

Washington, D.C.20231 **ETATS-UNIS D'AMERIQUE**

Date of mailing (day/month/year) in its capacity as elected Office 14 June 2000 (14.06.00)

International application No. Applicant's or agent's file reference PCT/GB99/03472 **PU3556/PCT**

International filing date (day/month/year) Priority date (day/month/year) 20 October 1999 (20.10.99) 22 October 1998 (22.10.98)

Applicant

DOW, Gordon, J. et al

X in the demand filed wit	th the International Preliminary Examining Authority on: 16 May 2000 (16.05.00)		
in a notice effecting lat	ter election filed with the International Bureau on:		
_			
The election X was			
was no		* 11 .4*	
	t f 19 months from the priority date or, where Rule 32 applic		it under
made before the expiration o			it under
made before the expiration o			it under
made before the expiration o			it under

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Olivia RANAIVOJAONA

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

	From the INTERNATIONAL BUREAU	
PCT	To:	
NOTIFICATION OF THE RECORDING OF A CHANGE (PCT Rule 92bis.1 and Administrative Instructions, Section 422) Date of mailing (day/month/year)	CRAWLEY, Karen Glaxo Wellcome plc Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN ROYAUME-UNI	
11 April 2001 (11.04.01)	L	
Applicant's or agent's file reference PU3556/PCT	IMPORTANT NOTIFICATION	
International application No. PCT/GB99/03472	International filing date (day/month/year) 20 October 1999 (20.10.99)	
The following indications appeared on record concerning: X the applicant X the inventor	the agent the common representative	
Name and Address RAJAGOPALAN, Rukmini Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park, NC 27709 United States of America	State of Nationality US US Telephone No. Facsimile No.	
:	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the the person the name X the add		
Name and Address RAJAGOPALAN, Rukmini GlaxoSmithKline c/o Corporate Intellectual Property Department Five Moore Drive	State of Nationality US US Telephone No.	
P.O. Box 13398 Research Triangle Park, NC 27709 United States of America	Facsimile No. Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
X the receiving Office	the designated Offices concerned	
the International Searching Authority the International Preliminary Examining Authority	the elected Offices concerned other:	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer I. Britel	
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38	

	From t	he INTERNATIO	NAL BL	JREAU
PCT	To:			
NOTIFICATION OF THE RECORDING OF A CHANGE (PCT Rule 92bis.1 and Administrative Instructions, Section 422) Date of mailing (day/month/year) 11 April 2001 (11.04.01)		CRAWLEY, Karen Glaxo Wellcome plc Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN ROYAUME-UNI		
Applicant's or agent's file reference				
PU3556/PCT		IMPORTANT	F NOTIF	FICATION
International application No.	1	nal filing date (day/r	-	ar)
PCT/GB99/03472	20 0	October 1999 (20.	.10.99)	
The following indications appeared on record concerning: X the applicant X the inventor	the ager	the	commor	n representative
Name and Address	-	State of Nationalit	Ϋ́	State of Residence
JOHNSON, Keith, Arthur Glaxo Wellcome Inc.		US Telephone No.		US
Five Moore Drive Research Triangle Park, NC 27709				
United States of America		Facsimile No.		
•		Teleprinter No.		
2. The International Bureau hereby notifies the applicant that the	ne following	change has been re	corded co	oncerning:
the person the name X the add	lress	the nationality		the residence
Name and Address		State of Nationality	y	State of Residence
JOHNSON, Keith, Arthur GlaxoSmithKline		US Telephone No.		US
c/o Corporate Intellectual Property Department Five Moore Drive		•		
P.O. Box 13398		Facsimile No.		
Research Triangle Park, NC 27709 United States of America		Teleprinter No.		
	}			
3. Further observations, if necessary:				
				<u>.</u>
4. A copy of this notification has been sent to:				
X the receiving Office		the designated	Offices ce	oncerned
the International Searching Authority	ا	X the elected Offi	ces conce	erned
the International Preliminary Examining Authority		other:		
The International Bureau of WIPO 34, chemin des Colombettes	Authorized	officer I. Brite	ı	
1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Telenhone	Nn · (41-22) 338 83 3	3 8	

	From th	ne INTERNATIONAL	BUREAU
PCT	To:		
NOTIFICATION OF THE RECORDING OF A CHANGE (PCT Rule 92bis.1 and Administrative Instructions, Section 422) Date of mailing (day/month/year) 11 April 2001 (11.04.01)	CRAWLEY, Karen Glaxo Wellcome plc Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN ROYAUME-UNI		
Applicant's or agent's file reference			
PU3556/PCT		IMPORTANT NO	OTIFICATION
International application No.	Internation	nal filing date (day/mont)	h/year)
PCT/GB99/03472	20 O	ctober 1999 (20.10.9	99)
The following indications appeared on record concerning: X the applicant X the inventor	the agen	t the com	nmon representative
Name and Address KELLY, Frances, Furr		US	US State of Residence
Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park, NC 27709 United States of America		Telephone No.	
Office diates of a money	1	Facsimile No.	
<u>. </u>		Teleprinter No.	
2. The International Bureau hereby notifies the applicant that th	e following	change has been recorde	ed concerning:
the person the name X the add	ress	the nationality	the residence
Name and Address		State of Nationality	State of Residence
KELLY, Frances, Furr GlaxoSmithKline c/o Corporate Intellectual		US Telephone No.	US
Property Department Five Moore Drive	ļ	,	
P.O. Box 13398 Research Triangle Park, NC 27709		Facsimile No.	
United States of America	ļ	Teleprinter No.	
3. Further observations, if necessary:			
G. Farther South Grand,			-
4. A copy of this notification has been sent to:			
X the receiving Office	Γ	the designated Offic	ces concerned
the International Searching Authority	Ī	The elected Offices o	concerned
the International Preliminary Examining Authority	<u> </u>	other:	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized	officer I. Britel	
Facsimile No : (41.22) 740 14 35	Telephone	No · (41.22) 338 83 38	

	From	the INTERNATIONAL I	BUREAU
PCT			
NOTIFICATION OF THE RECORDING OF A CHANGE (PCT Rule 92bis.1 and Administrative Instructions, Section 422) Date of mailing (day/month/year) 11 April 2001 (11.04.01)	CRAWLEY, Karen Glaxo Wellcome pic Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN ROYAUME-UNI		
Applicant's or agent's file reference		IMPORTANT NOT	TEICATION
PU3556/PCT			IIICATION
International application No. PCT/GB99/03472	1	onal filing date (day/month/) October 1999 (20.10.99	
1. The following indications appeared on record concerning:			
X the applicant X the inventor	the age	nt the comm	on representative
Name and Address		State of Nationality	State of Residence
LATHROP, Robert, William Dow Pharmaceutical Science		US	US
1330A Redwoodway		Telephone No.	· · · · · · · · · · · · · · · · · · ·
Petaluma, CA 94954 United States of America			
Times of the original of the o		Facsimile No.	
			* · · · · · · · · · · · · · · · · · · ·
•		Teleprinter No.	
2. The leteraction of December 1			
2. The International Bureau hereby notifies the applicant that		_ ,	-
the person the name X the ad	dress	the nationality	the residence
Name and Address		State of Nationality	State of Residence
LATHROP, Robert, William GlaxoSmithKline		US	US
c/o Corporate Intellectual		Telephone No.	
Property Department Five Moore Drive			
P.O. Box 13398		Facsimile No.	
Research Triangle Park, NC 27709 United States of America	l		
Officed States of Afficia		Teleprinter No.	
3. Further observations, if necessary:			
4. A copy of this notification has been sent to:			
X the receiving Office	Г	the designated Offices	concerned
the International Searching Authority	F	X the elected Offices cond	
the International Preliminary Examining Authority	Ļ	=	Jerrieu
LJ memorial resimilary examining Authority	L	other:	
The later with the second	Authorized	officer	
The International Bureau of WIPO 34, chemin des Colombettes			
1211 Geneva 20, Switzerland		I. Britel	
acsimile No.: (41-22) 740.14.35	Telephone I	No.: (41-22) 338.83.38	

Form PCT/IB/306 (March 1994)

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference FOR FURTHER see Notification of Transmittal of International Search Report							
PU3556/PCT (Form PCT/ISA/220) as well as, where applicable, item 5 below							
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)					
PCT/GB 99/03472	20/10/1999	22/10/1998					
Applicant							
GLAXO GROUP LIMITED et al	GLAXO GROUP LIMITED et al.						
This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.							
This International Search Report consists	of a total of 3 sheets.						
· .	of a total of sheets. a copy of each prior art document cited in this	report.					
Basis of the report With regard to the language the	international search was carried out on the bas	is of the international application in the					
language in which it was filed, unl	ess otherwise indicated under this item.	is of the international application in the					
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of the	ne international application furnished to this					
b. With regard to any nucleotide an	d/or amino acid sequence disclosed in the in	ternational application, the international search					
was carried out on the basis of the contained in the internation	nal application in written form.						
filed together with the inte	rnational application in computer readable form	1.					
furnished subsequently to	this Authority in written form.						
	this Authority in computer readble form.						
the statement that the sub- international application a	sequently furnished written sequence listing do s filed has been furnished.	pes not go beyond the disclosure in the					
the statement that the info furnished	ormation recorded in computer readable form is	identical to the written sequence listing has been					
2. Certain claims were four	nd unsearchable (See Box I).						
3. Unity of invention is lack	king (see Box II).	·					
4 NASAb represed to the state							
4. With regard to the title, The text is approved as su	hmitted by the applicant						
	hed by this Authority to read as follows:						
	the by the Mationty to read as ionows.						
5. With regard to the abstract,							
the text has been establis	the text is approved as submitted by the applicant. the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.						
6. The figure of the drawings to be published with the abstract is Figure No.							
as suggested by the applicant. None of the figures.							
because the applicant faile	ed to suggest a figure.	<u> </u>					
because this figure better	characterizes the invention.						

International Application No T/GB 99/03472

A. CLASSIFICATION OF SUBJECT 1 IPC 7 A61K31/57

A61K31/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\label{eq:minimum} \begin{array}{ll} \text{Minimum documentation searched (classification system followed by classification symbols)} \\ IPC 7 & A61K \end{array}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUM	C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.				
X	WO 92 14472 A (GLAXO GROUP LTD) 3 September 1992 (1992-09-03) example 1 page 2, line 7 claims	1,5,18,				
Υ .	EP 0 042 827 A (AKTIEBOLAGET DRACO) 30 December 1981 (1981-12-30) the whole document/	1,2, 5-11,14, 18,21,22				

X Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 26 January 2000	Date of mailing of the international search report $04/02/2000$
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Pelli Wablat, B

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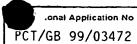
International Application No T/GB 99/03472

	tion) DOCUMENTS CON ED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to daim No.
Y	BLEEHEN S.S ET AL.: BRITISH JOURNAL OF DERMATOLOGY, vol. 133, no. 4, - 1995 pages 592-597, XP000864345 page 592, left-hand column, last paragraph page 593, left-hand column, line 33 - line 38 page 594, line 8 - line 18	1,2, 5-11,14, 18,21,22
	SPENCER CAROLINE M: ET AL: BIODRUGS, vol. 7, no. 4, - 1997 pages 318-334, XP000864346 the whole document	1,2,5, 18,21,22
	-	

Information on patent family members

International Application No CT/GB 99/03472

Patent document cited in search repo	nt (Publication date	1	Patent family member(s)	Publication date
WO 9214472	Α	03-09-1992	AT	114244 T	15-12-1994
			AU	1277792 A	15-09-1992
			CA	2104677 A	23-08-1992
			DE	69200711 D	05-01-1995
			DK	573492 T	09-01-1995
			EP	0573492 A	15-12-1993
			ES	2064166 T	16-01-1995
			GR	3015014 T	31-05-1995
			MX	9200728 A	01-10-1992
EP 042827	Α	30-12-1981	DD	159736 A	06-04-1983
			DK	262681 A	20-12-1981
			ES	503132 A	16-04-1982
			FI	811745 A	20-12-1981
			GR	74568 A	29-06-1984
			JP	57031700 A	20-02-1982
			NO	812075 A	21-12-1981
			PT	73215 A,B	01-07-1981
			SE	8004580 A	20-12-1981
			US	4363806 A	14-12-1982
			ZA	8103465 A	30-06-1982



		1 0 1 / 0	
A. CLASSI IPC 7	FICATION OF SUBJECT MATTER A61K31/57 A61K7/48 A61K31/	56	
According to	o International Patent Classification (IPC) or to both national classific	cation and IPC	
	SEARCHED		
Minimum do IPC 7	ocumentation searched (classification system tollowed by classificat A61K	ion symbols)	
Documenta	tion searched other than minimum documentation to the extent that	such documents are included in the	fields searched
	ata base consulted during the international search (name of data ba	ase and, where practical, search ten	ms used)
	ENTS CONSIDERED TO BE RELEVANT		
Category ²	Citation of document, with indication, where appropriate, of the re	levant passages	Relevant to claim No.
X	WO 92 14472 A (GLAXO GROUP LTD) 3 September 1992 (1992-09-03) example 1 page 2, line 7 claims		1,5,18, 21,22
Y	EP 0 042 827 A (AKTIEBOLAGET DRACO) 30 December 1981 (1981-12-30) the whole document		1,2, 5-11,14, 18,21,22
		-/	
X Furth	ner documents are listed in the continuation of box C.	X Patent family members ar	re listed in annex.
"A" docume consid "E" earlier of filing d. "L" docume which in citation "O" docume other of the course of the cour	nt which may throw doubts on priority claim(s) or is cited to establish the publication date of another in or other special reason (as specified) entreferring to an oral disclosure, use, exhibition or	the international filing date lict with the application but ole or theory underlying the ce; the claimed invention or cannot be considered to in the document is taken alone ce; the claimed invention we an inventive step when the e or more other such docuge obvious to a person skilled	
	5 January 2000	Date of mailing of the internation $04/02/2000$	onar search report
Name and m	В		



		PCT/GB 99/03472
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category :	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BLEEHEN S.S ET AL.: BRITISH JOURNAL OF DERMATOLOGY, vol. 133, no. 4, - 1995 pages 592-597, XP000864345 page 592, left-hand column, last paragraph page 593, left-hand column, line 33 - line 38 page 594, line 8 - line 18	1,2, 5-11,14, 18,21,22
Д	SPENCER CAROLINE M: ET AL: BIODRUGS, vol. 7, no. 4, - 1997 pages 318-334, XP000864346 the whole document	1,2,5, 18,21,22
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2

ation on patent family members

.ional Application No PCT/GB 99/03472

Patent document cited in search report		Publication date	Patent family member(s)		Publication date	
WO 9214472	Α	03-09-1992	AT	114244 T	15-12-1994	
			AU	1277792 A	15-09-1992	
			CA	2104677 A	23-08-1992	
			DE	69200711 D	05-01-1995	
			DK	573492 T	09-01-1995	
			EP	0573492 A	15-12-1993	
			ES	2064166 T	16-01-1995	
			GR	3015014 T	31-05-1995	
			MX	9200728 A	01-10-1992	
EP 042827	Α	30-12-1981	DD	159736 A	06-04-1983	
			DK	262681 A	20-12-1981	
			ES	503132 A	16-04-1982	
			FI	811745 A	20-12-1981	
			GR	74568 A	29-06-1984	
			JP	57031700 A	20-02-1982	
			NO	812075 A	21-12-1981	
			PT	73215 A,B	01-07-1981	
			SE	8004580 A	20-12-1981	
			US	4363806 A	14-12-1982	
			ZA	8103465 A	30-06-1982	

From the INTERNATIONAL SEAR	CHING AUTHORITY	P	CT
To: GLAXO WELLCOME PLC Glaxo Wellcome House Attn. CRAWLEY,KAREN Berkeley Avenue Greenford Middlesex UB6 ONN UNITED KINGDOM	Global Intellech: RECEIVED 1 0 FEB 20 ACTION DATE	OR THE INTERNATION OR THE INTERN	OF TRANSMITTAL OF ONAL SEARCH REPORT IE DECLARATION OT Rule 44.1)
		04/02	2/2000
Applicant's or apen's file reference		FOR FURTHER ACTION	See paragraphs 1 and 4 below
PU3556/PCT International application No. PCT/GB 99/03472		International filing date	0/1999
Applicant			
GLAXO GROUP LIMITED et	al.		
Filing of amendments and The applicant is entitled, if he When? The time limit for fil International Searc Where? Directly to the In 34 12 Fa	statement under Article 19: e so wishes, to amend the claims	Report has been established and soft the International Application by 2 months from the date of trainals, see the notes on the accompanying sheet.	(see Rule 46):
2. The applicant is hereby notifind Article 17(2)(a) to that effect	ied that no International Search is transmitted herewith.	Report will be established and	that the declaration under
	the desirion thereon has been	nal fee(s) under Rule 40.2, the a n transmitted to the International test and the decision thereon to	Bureau together with the
no decision has been	made yet on the protest; the app	olicant will be notified as soon as	a decision is made.
Shortly after 18 months from the fifthe applicant wishes to avoid priority claim, must reach the In completion of the technical prep. Within 19 months from the priorit wishes to postpone the entry in	or postpone publication, a notice ternational Bureau as provided parations for international publicate date, a demand for internation to the national phase until 30 mo	in Rules 90 <i>bis</i> .1 and 90 <i>bis</i> .3, reation. all preliminary examination must onthe from the priority date (in so	be filed if the applicant one Offices even later).
Within 20 months from the priority before all designated Offices who priority date or could not be element.	ty date, the applicant must perform hich have not been elected in the cted because they are not bound	ie delitaria di ili a later election.	into the national phase within 19 months from the
Name and mailing address of the Inte	emational Searching Authority	Authorized officer	

Doreen Golze

Form PCT/ISA/220 (July 1998)

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Express Mail Label EL395942518US

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international poulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

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Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Bule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

Haw?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) 'the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 *Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
 claims 30, 33 and 35 unchanged; new claims 49 to 51 added.*
- (Where originally there were 15 claims and after amendment of all claims there are 11):
 "Claims 1 to 15 replaced by amended claims 1 to 11."
- 3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
 "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- [Where various kinds of amendments are made]:
 "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

it must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.



(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	(Form PCT/ISA/2	of Transmittal of International Search Report 20) as well as, where applicable, item 5 below.
PU3556/PCT	ACTION	I to the Date of the Contract to the Contract
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/GB 99/03472	20/10/1999	22/10/1998
Applicant		
GLAXO GROUP LIMITED et al		
deaxo dicor Elitito co di		
This International Search Report has bee according to Article 18. A copy is being tr	n prepared by this International Searching Aut ansmitted to the International Bureau.	hority and is transmitted to the applicant
This International Search Report consists It is also accompanied by	of a total of3 sheets.	s report.
1. Basis of the report		
a. With regard to the language, the language in which it was filed, un	international search was carried out on the ba less otherwise indicated under this item.	sis of the international application in the
Authority (Rule 23.1(b)).	vas carried out on the basis of a translation of	
was carried out on the basis of the	ne sequence listing:	nternational application, the international search
	onal application in written form.	
· — ·	emational application in computer readable for	rm.
furnished subsequently t	o this Authority in written form.	
furnished subsequently t	o this Authority in computer readble form.	
international application	bsequently furnished written sequence listing as filed has been furnished.	•
the statement that the in furnished	formation recorded in computer readable form	is identical to the written sequence listing has been
	und unsearchable (See Box I).	•
3. Unity of invention is la	cking (see Box II).	
4. With regard to the title,		
1	submitted by the applicant.	
the text has been estable	ished by this Authority to read as follows:	
5. With regard to the abstract,		
TX the text is approved as s	submitted by the applicant.	
I	ished, according to Rule 38.2(b), by this Authone date of mailing of this international search re	ority as it appears in Box III. The applicant may, eport, submit comments to this Authority.
6. The figure of the drawings to be pu	blished with the abstract is Figure No.	All and the figures
as suggested by the ap		None of the figures.
	ailed to suggest a figure.	
because this figure better	er characterizes the invention.	

International Application No B 99/03472

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/57 A61K7748

A61K31/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
WO 92 14472 A (GLAXO GROUP LTD) 3 September 1992 (1992-09-03) example 1 page 2, line 7 claims	1,5,18, 21,22
EP 0 042 827 A (AKTIEBOLAGET DRACO) 30 December 1981 (1981-12-30)	1,2, 5-11,14, 18,21,22
-/	
	example 1 page 2, line 7 claims EP 0 042 827 A (AKTIEBOLAGET DRACO)

N		
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	
"E" earlier document but published on or after the international filling date	r after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-	
"O" document referring to an oral disclosure, use, exhibition or other means	ments, such combination being obvious to a person skilled in the art.	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family	
Date of the actual completion of the international search	Date of mailing of the international search report	
26 January 2000	04/02/2000	
Name and mailing address of the ISA	Authorized officer	
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk		
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.	Pelli Wablat, B	

Fax: (+31-70) 340-3016

2

International Application No POSS 99/03472

C.(Continuation) DOCUMENTS CONSIDER BE RELEVANT						
ategory *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to c	laim No.			
Y	BLEEHEN S.S ET AL.: BRITISH JOURNAL OF DERMATOLOGY, vol. 133, no. 4, - 1995 pages 592-597, XP000864345 page 592, left-hand column, last paragraph page 593, left-hand column, line 33 - line 38 page 594, line 8 - line 18	1,2 5-1 18,	, 1,14, 21,22			
A	SPENCER CAROLINE M: ET AL: BIODRUGS, vol. 7, no. 4, - 1997 pages 318-334, XP000864346 the whole document	1,2 18,	,5, 21,22			

2

Information on patent family members

P(B 99/03472

Patent document cited in search report		Publication date		ratent family member(s)	Publication date
WO 9214472	Α	03-09-1992	AT	114244 T	15-12-1994
NO 322			AU	1277792 A	15-09-1992
			CA	2104677 A	23-08-1992
			DE	69200711 D	05-01-1995
			DK	573492 T	09-01-1995
			EP	0573492 A	15-12-1993
			ES	2064166 T	16-01-1995
			GR	3015014 T	31-05-1995
		•	MX	9200728 A	01-10-1992
EP 042827		30-12-1981	DD	159736 A	06-04-1983
Er 042027	^	30 12 1301	DK	262681 A	20-12-1981
			ES	503132 A	16-04-1982
	٠		FĬ	811745 A	20-12-1981
			GR	74568 A	29-06-1984
			JP	57031700 A	20-02-1982
			NO	812075 A	21-12-1981
			PT	73215 A,B	01-07-1981
		•	SE	8004580 A	20-12-1981
			US	4363806 A	14-12-1982
			ZA	8103465 A	30-06-1982

EUROP. PRIENTENT COOPERATION TREATY

NR.262

S. 1

From the

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY (FOT REC 20 APR 20

To:

FILLER, Wendy A. **GLAXO WELLCOME PLC** Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN

GRANDE BRETAGNE

International application No.

PCT/GB99/03472

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY **EXAMINATION REPORT** (PCT Rule 71.1)

gnifism to eta0

(day/month/year)

06.03.2001

Applicant's or agent's file reference

PU3556/WO

international filing date (day/month/year)

20/10/1999

IMPORTANT NOTIFICATION

Priority date (day/month/year) 22/10/1998

Applicant

GLAXO GROUP LIMITED et al.

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

Authorized officer

European Patent Office D-80298 Munich

Tel. +49 89 2399 - 0 Tx: 523656 epimu d

Fax: +49 89 2399 - 4465

Senkel, H

Tel.+49 89 2399-8071



Form PCT/IPEA/416 (July 1892)

NR.262 S.2



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

In.	56/WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PCT/G	lonal application No. 3B99/03472	International filing date (day/month/) 20/10/1999	year) Priority date (day/month/year)
A61K3	ional Patent Classification 11/57	(IPC) or national classification and IPC	22/10/1998
Applican			
GLAXI	O GROUP LIMITED	et al.	
1. This and	s international prelimin I is transmitted to the a	ary examination report has been prepared bupplicant according to Article 36.	y this International Preliminary Examining Author
		a total of 7 sheets, including this cover she	
	This report is also accident amended and artificial (see Rule 70.16 and S	companied by ANNEXES, i.e. sheets of the companied by ANNEXES, i.e. sheets of the companies of the basis for this report and/or sheets confection 607 of the Administrative instructions	description, claims and/or drawings which have taining rectifications made before this Authority
	e annexes consist of	· · · · · · · · · · · · · · · · · · ·	s under the PCT).
		a Coldi of Sheets.	
This	Basis of the rep	ions relating to the following items:	
1	Basis of the rep Priority Non-establishm	port	
II II I	Basis of the rep Priority Non-establishm Lack of unity of	port nent of opinion with regard to novelty, inventi Invention	
1 11 111	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state	nent of opinion with regard to novelty, invention	
II II I	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state	nent of opinion with regard to novelty, invention invention of the superior of	ve step and Industrial applicability elty, Inventive step or industrial applicability;
\rm \text{\rm \rm \text{\rm \text{\rm \text{\rm \text{\rm \rm \text{\rm \rm \text{\rm \rm \text{\rm \rm \rm \rm \text{\rm \rm \rm \rm \rm \rm \rm \rm \rm \rm	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state citations and ex Certain docume Certain defects	nent of opinion with regard to novelty, invention invention of the statement of the superting such statement ents cited in the international application	
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\(\) \(\) \(\) \(\) \(\) \(\) \(\) \(\)	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state citations and ex Certain docume Certain defects Certain observat	nent of opinion with regard to novelty, invention invention of the statement of the superting such statement ents cited in the international application	
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	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state citations and ex Certain decume Certain defects Certain observat	pent of opinion with regard to novelty, invention invention of planations suporting such statement ents cited in the international application on the international application Date of complete in the complete of complete comple	elty, inventive step or industrial applicability;
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IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	Basis of the rep Priority Non-establishm Lack of unity of Reasoned state citations and ex Certain docume Certain detects Certain observat	pent of opinion with regard to novelty, invention intent under Article 35(2) with regard to novel planations suporting such statement ents cited in the international application tions on the international application Date of complete of the complete of	elty, Inventive step or industrial applicability;

NR.262 5.3



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03472

		Basis of the repo	
	1.	This report has be response to an invalue the report since the Description, page	en drawn on the basis of (substitute sheets which have been furnished to the receiving Office in entation under Article 14 are referred to in this report as "originally filed" and are not annexed to so so so to annexed to secondary.):
		1-19	as originally filed
		Claims, No.:	
		1-24	as originally filed
	2.	With regard to the la	anguage, all the elements marked above were available or furnished to this Authority in the
		. Hoose clements wer	e available or furnished to this Authority in the following language: . which is:
	_	the language of	a translation furnished for the purposes of the international search (under Rule 23.1(b)).
	[
		the language of	a translation furnished for the purposes of international preliminary examination (under Rule
	3. V in	Vith regard to any nuternational prelimina	eclectide and/or amino acid sequence disclosed in the international application, the ary examination was carried out on the basis of the sequence listing:
		contained in the i	nternational application in written form.
		filed together with	the international application in computer readable form.
		furnished subseq	uently to this Authority in written form.
		iornisnea subseqi	uently to this Authority is computed and the
	_	the international a	It the subsequently furnished written sequence listing does not go beyond the disclosure is
		listing has been fu	it the information recorded in computer readable form is identical to the written sequence
4.	The	e amendments have	resulted in the cancellation of:
		the description,	Pages:
		the claims.	Nos.:
		the drawings,	sheets:
5.		This report has bee considered to go be	on established as if (some of) the amendments had not been made, since they have been eyond the disclosure as filed (Rule 70.2(c));

NR. 262

5.4



INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

International application No. PCT/GB99/03472

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this

	-	and any and any	wexed to this
	6. Additional observations	if necessary:	
	obvious), or to be Indus	ppinion with regard to novelty, inventive step and industrial applicabiling claimed invention appears to be novel, to involve an inventive step (to be its applicable have not been examined in respect of:	ty ∋ rion-
	☐ the entire internatio ☑ - claims Nos. 21-24.	al application.	
	because:		
	the said international does not require an see separate sheet	application, or the said claims Nos. 21-24 relate to the following subject maternational preliminary examination (specify):	itler which
	the description, clair that no meaningful o	s or drawings (<i>indicate particular element</i> s <i>below</i>) or said claims Nos. are s inion could be formed (<i>specify</i>):	30 undear
		ims Nos. are so inadequately supported by the description that no meaning	noinigo luit
	no international searce	report has been established for the sald claims Nos	
2	. A meaninaful international	preliminary examination report cannot be carried out due to the failure of the elisting to comply with the standard provided for in Annex C of the Adminis	a nucleotide frative
	the written form has n	t been furnished or does not comply with the standard.	
	☐ the computer readable	form has not been furnished or does not comply with the standard.	
V.	Reasoned statement und	r Article 35(2) with regard to novelty, inventive step or industrial applic supporting such statement	rahilih
۱.	Statement		-ability;
	Novelty (N)	Yes: Claims 2-4, 6-13, 15-17, 19, 20, 23, 24 No: Claims 1, 5, 14, 18, 21, 22	
	Inventive step (IS)	Yes: Claims No: Claims 1-24	
	Industrial applicability (IA)	Yes: Claims see sections III and V	

NR. 262 5.5





INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

International application No. PCT/GB99/03472

No: Claims

2. Citations and explanations see separate sheet

INTERNATIONAL PR **EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03472

SECTION III:

Claims 21 to 24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V:

Prior art

Reference is made to the following documents:

D1 (WO 92 14472 A) relates to topical pharmaceutical compositions containing fluticasone propionate and oxiconazole as active ingredients (p. 1, §1).

D2 (EP-A-0 042 827) is concerned with pharmaceutical compositions for topical application containing a corticosteroid as the active ingredient (p. 1, §1).

D3 (BLEEHEN S.S. et al.) compares the efficacy and safety of once-daily with twicedaily applications of a 0.05% cream formulation of fluticasone propionate in the treatment of atopic eczema in adults and children (abstract).

D4 (SPENCER C.M. et al.) discloses a review of fluticasone propionate, its pharmacological properties and therapeutic uses in the treatment of dermatological disorders (title).

Novelty

The subject-matter of claims 1, 5, 14, 18, 21 and 22 is not new in the sense of Article 33 (2) PCT.

The following claims are not new over the following documents with their cited



INTERNATIONAL PRELIMINARY **EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03472

Claim 1: D1: example 1 Claim 5: D1: example 1 Claim 14: D1: example 1 Claim 18: D1: example 1

Claim 21: D1: example 1, p. 1, §3 and 4 Claim 22: D1: example 1, p. 1, §3 and 4

While D2 discloses the same auxiliary components as present claim 1 (p. 2, §3 to p. 3, §3), it is silent to the active substance fluticasone. Therefore, D2 does not anticipate novelty of present claims 1 to 24.

D3 discloses the auxiliary components as claimed in claim 1 (p. 593, left col., §4), but it is silent to the percentage of the said components. Further, it describes well the treatment of skin diseases (atopic eczema) with fluticasone (abstract; p. 592, left col. §1; p. 594, right col. §2). D3 does not anticipate novelty of present claims 1 to 24.

D4 gives an overview to the active substance fluticasone and its uses.

Inventive step

The subject-matter of claims 1 to 24 does not involve an inventive step in the sense of Article 33 (3) PCT.

For claims 1, 5, 14, 18, 21 and 22 the following applies:

Even if the applicant is able to establish novelty it cannot be seen that any particular aspect of the application as filed would involve an inventive step under Article 33 (3) PCT in the light of the relevant prior art.

For claims 2, 6, 7, 9, 12, 13, 15 to 17 the following applies:

The additional features of said claims can be determined by routine experiments and are therefore not inventive in the sense of Article 33 (3) PGT.

For claims 3 and 4 the following applies:

The additional features of claims 3 and 4 can be determined as alternatives and are therefore not inventive in the sense of Article 33 (3) PCT.



INTERNATIONAL PR **EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03472

For claims 8, 10, 11, 19, 20, 23 and 24 the following applies:

EUROP. PATENTAMT

The additional features of claims 8, 10, 11, 19, 20, 23 and 24 can be determined by routine experiments and are therefore not inventive in the sense of Article 33 (3) PCT.

Industrial applicability

For the assessment of the present claims 21 to 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

For the EPO the following applies:

Claims 14 and 15 are directed to the use of a medicament for the inhibition of a biological mechanism; such a use cannot be patented, since it is not considered as relating to a therapeutic application in the meaning of the decision of the Enlarged Board of Appeal Gr.05/83, O.J. 1/1983, page 64, according to which only the use of the composition of claim 1 for the manufacture of a medicament for a new and inventive therapeutic application could be patentable.

Information on patent family members

International Application No

Patent document cited in search report		Publication date		ratent family member(s)	Publication date
WO 9214472		03-09-1992	AT	114244 T	15-12-1994
WU 32144/2	^	33 33 237=	AU	1277792 A	15-09-1992
			CA	2104677 A	23-08-1992
			DE	69200711 D	05-01-1995
			DK	573492 T	09-01-1995
			EP	0573492 A	15-12-1993
			ES	2064166 T	16-01-1995
			GR	3015014 T	31-05-1995
		·	MX	9200728 A	01-10-1992
EP 042827	 A	30-12-1981	 DD	159736 A	06-04-1983
Er 042027	^	30 12 1301	DK	262681 A	20-12-1981
			ES	503132 A	16-04-1982
	•		FΙ	811745 A	20-12-1981
			GR	74568 A	29-06-1984
			JP	57031700 A	20-02-1982
:			NO.	812075 A	21-12-1981
			PT	73215 A,B	01-07-1981
			SE	8004580 A	20-12-1981
			ÜS	4363806 A	14-12-1982
			ZA	8103465 A	30-06-1982

REQUEST

The undersigned requests that the present International application be processed

1	For receiving ice use only
	International Application No.
	Intermational Paling Dates C' (1 2 2003
	Name of receiving Office and "PCT International Application"
ı	Applicant's or agent's file reference

according to the Patent Cooperation Treaty (if desired) (12 characters maximum) PU3556/PCT TITLE OF INVENTION Box No. I Fluticasone Lotion Having Improved Vasoconstrictor Activity APPLICANT Box No. II Name and address: (Family name followed by given name; for a legal entity, full official This person is also inventor. designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is Telephone No. 0171 493 4060 indicated below). axo Group Limited Facsimile No. 0181 966 8838 Glaxo Wellcome House Teleprinter No. 25456 Berkeley Avenue Greenford, Middlesex UB6 ONN, GB State (i.e. country) of residence: State (i.e. country) of nationality: GB the States indicated in the the United States all designated States except all designated This person is applicant Supplemental Box of America only the United States of America for the purposes of: FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS Box No. III Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address This person is: indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is applicant only indicated below.) DOW, Gordon J applicant and inventor Dow Pharmaceutical Science 1330A Redwoodway inventor only (If this check-box aluma is marked, do not fill in below.) **CA 9454** US State (i.e. country) of residence: State (i.e. country) of nationality: US US the States indicated in the United States all designated States except all designated This person is applicant the Supplemental Box of America only the United States of America for the purposes of: States Further applicants and/or (further) inventors are indicated on a continuation sheet. AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE The person identified below is hereby/has been appointed to act on behalf common representative X agent of the applicant(s) before the competent International Authorities as: Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country). Telephone No.: 0171-493-4060 CRAWLEY, Karen Facsimile No.: 0181-966-8838 Glaxo Wellcome plc Glaxo Wellcome House, Berkeley Avenue Greenford, Middlesex Teleprinter No.: 25456 UB6 0NN GB Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to o which correspondence should be sent.

Express Mail Label EL395942518US

ly 1998)

See Notes to the request form

Sheet No .2	
Continuation of Box No. III FURTHER A CONTINUATION OF BOX NO. III FURT	TOP
If none of the following sub-boxes is used, this sheet is not to be included	ded in the request.
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) JOHNSON, Keith Arthur Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park North Carolina 27709	This person is: applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)
US State (i.e. country) of nationality: State (i.e. country) of resi	idence: US
This person is applicant [] All (ESIGNAID) [] all (ESIGNAID) States except	nited States nerica only The States indicated in The Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this is the applicant's State (that is, country) of residence if no State of residence is indicated below.) KELLY, Frances Furr Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park North Carolina 27709 US	This person is: applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)
State (i.e. country) of nationality: State (i.e. country) of res	idence: US
This mercen is confiled to the first think the first think the second of the first think the f	nited States The States indicated in The Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) LATHROP, Robert William Dow Pharmaceutical Science 1330A Redwoodway Laluma CA 9454	This person is: applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)
State (i.e. country) of nationality: State (i.e. country) of res	sidence: US
	Inited States The States indicated in The Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (tht is, country) of residence if no State of residence is indicated below.) RAJAGOPALAN, Rukmini Glaxo Wellcome Inc. Five Moore Drive Research Triangle Park North Carolina 27709, US State (i.e. country) of residence is indicated below.)	This person is: applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)
US This person is applicant all designated all designated States except the U	hited States
for the purposes of: States the United States of America of Ar	merica only
Further applicants and/or (further) inventors are indicated on a continuation sheet.	

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		- Dr. A.	Cur	itzerla	nd and Liechtenstein, CY Cyprus, DE Germany,
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\square	HR	Croatia			Trinidad and Tobago
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	IS	Iceland		UZ	Uzbekistan
	JP	Japan	\square	VN	Viet Nam
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Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) and other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

. •		Sheet No .4		
Box No. VI PRIORIT	TY CLAIM	Further priority	claims are indicated in th	e Supplemental Box
DUALITY I I I I I I I I I I I I I I I I I I			Where earlier application in regional application:	s International application:
Filing Date of Earlier Application (day/month/year)	Number Of earlier application	national application: re country	regional Office	Receiving Office
item (1) (22.10.98)	9823036.0	GB	!	
22 October 1998 item (2)				
· item (3)				
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Choice of International Sea (if two or more International Sea empetent to carry out the international Sea ority chosen; the two-letter	arching Authorities are national search, indicate the	Request to use results of ea search has been carried out by Date (day/month/year)	or requested from the Interi	national Searching Authority): intry (or regional office)
Box. VIII CHEC	CK LIST; LANGUA	E OF FILING		
This international applicati	on contains This is	ternational application is accom	npanied by the item(s) m	arked below:
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request	: 4	copy of general power of attor	rney; reference number, i	f any:
description (excluding	4. 🗆	statement explaining lack of s	signature	
sequence listing part)	: 19 5. - : 4 6. -	priority document(s) identified translation of international app	onlication into (language):	s). :
claims	1 7.	separate indications concerning	ng deposited microorgani	sm or other biological
abstract drawings		material		
sequence listing part	8. 🗖	nucleotide and/or amino acid other (specify):	sequence listing in comp	uter readable form
of description	:	outer (specify).		
Total number of sheets	: 28	Language of filing	of the	
Figure of the drawings wi should accompany the abs	hich tract:	International applic	cation: English	
	ATURE OF APPLIC	ANT OR AGENT		
to each signature, indicate	the name of the person signi	g and the capacity in which the person	on signs (if such capacity is not	obvious from reading the
request).				
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Karen CRAWLEY Agent for the Applican	nts			
		For receiving Office use on	nly	2. Drawings
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REC'D 09 MAR 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference		See Notification of Transmittal of International
PU3556/WO	FOR FURTHER ACTION	Preliminary Examination Report (Form PCT/IPEA/416)
International application No.	International filing date (day/month)	/year) Priority date (day/month/year)
PCT/GB99/03472	20/10/1999	22/10/1998
International Patent Classification (IPC) A61K31/57	or national classification and IPC	
Applicant		
GLAXO GROUP LIMITED et al.		
This international preliminary e and is transmitted to the applic	examination report has been prepared tant according to Article 36.	by this International Preliminary Examining Authority
2. This REPORT consists of a tot	al of 7 sheets, including this cover sh	neet.
been amended and are the	panied by ANNEXES, i.e. sheets of the e basis for this report and/or sheets on on 607 of the Administrative Instruction	e description, claims and/or drawings which have ontaining rectifications made before this Authority ons under the PCT).
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These annexes consist of a tol	lai Vi Sileets.	
3. This report contains indications	s relating to the following items:	
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1 ⊠ Basis of the report	I .	
II ☐ Priority	A of aciding with appeal to povolty in	continue stan and industrial applicability
<u> </u>		rentive step and industrial applicability
IV Lack of unity of inv		novelty, inventive eten or industrial applicability:
V ⊠ Reasoned stateme citations and expla	ent under Article 35(2) with regard to landtions suporting such statement	novelty, inventive step or industrial applicability;
VI Certain document		
VII Certain defects in	the international application	
	ons on the international application	
Date of submission of the demand	Date of	completion of this report
16/05/2000	06.03.20	001
Name and mailing address of the intem preliminary examining authority:	ational Authoriz	eed officer
European Patent Office D-80298 Munich	Heller,	
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Telephone No. +49 89 2399 8746

International application No. PCT/GB99/03472

I. Basis of the report

1.	resp the i	onse to an invitatio	awn on the basis of (substitute sheets which have been furnished to the receiving Office in nunder Article 14 are referred to in this report as "originally filed" and are not annexed to not contain amendments (Rules 70.16 and 70.17).):
	1-19)	as originally filed
	Clai	ms, No.:	
	1-24	ŀ	as originally filed
2.	With lang	n regard to the lang Juage in which the i	uage, all the elements marked above were available or furnished to this Authority in the nternational application was filed, unless otherwise indicated under this item.
	The	se elements were a	vailable or furnished to this Authority in the following language: , which is:
		the language of a t	ranslation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pu	blication of the international application (under Rule 48.3(b)).
		the language of a t 55.2 and/or 55.3).	ranslation furnished for the purposes of international preliminary examination (under Rule
3.	With	n regard to any nuc rnational preliminar	leotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:
		contained in the in	ternational application in written form.
		filed together with	the international application in computer readable form.
		furnished subsequ	ently to this Authority in written form.
		furnished subsequ	ently to this Authority in computer readable form.
			t the subsequently furnished written sequence listing does not go beyond the disclosure in oplication as filed has been furnished.
		The statement tha listing has been fu	t the information recorded in computer readable form is identical to the written sequence rnished.
4.	The	amendments have	resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:
		the drawings,	sheets:
5.			en established as if (some of) the amendments had not been made, since they have been beyond the disclosure as filed (Rule 70.2(c)):



(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6.	Add	litional observations, if ne	cessary	/ :	
II.	Nor	n-establishment of opini	ion with	n regard t	to novelty, inventive step and industrial applicability
۱.	obvi		applica	ble have	appears to be novel, to involve an inventive step (to be non- not been examined in respect of:
		claims Nos. 21-24.	ррпсан	on.	
ре	caus	se:			
	Ճ				eaid claims Nos. 21-24 relate to the following subject matter which eary examination (<i>specify</i>):
		the description, claims of that no meaningful opini			eate particular elements below) or said claims Nos. are so unclear ed (specify):
		the claims, or said claim could be formed.	s Nos.	are so in	adequately supported by the description that no meaningful opinion
		no international search	report h	as been e	established for the said claims Nos
2.	and				nation report cannot be carried out due to the failure of the nucleotide with the standard provided for in Annex C of the Administrative
		the written form has not	been fu	ırnished d	or does not comply with the standard.
		the computer readable f	orm has	s not bee	n furnished or does not comply with the standard.
V.		asoned statement under ations and explanations			ith regard to novelty, inventive step or industrial applicability;
1.	Stat	tement			
	Nov	velty (N)	Yes: No:		2-4, 6-13, 15-17, 19, 20, 23, 24 1, 5, 14, 18, 21, 22
	inve	entive step (IS)	Yes: No:	Claims Claims	1-24
	Indi	ustrial applicability (IA)	Yes:	Claims	see sections III and V





International application No. PCT/GB99/03472

No: Claims

2. Citations and explanations see separate sheet

SECTION III:

Claims 21 to 24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V:

Prior art

Reference is made to the following documents:

D1 (WO 92 14472 A) relates to topical pharmaceutical compositions containing fluticasone propionate and oxiconazole as active ingredients (p. 1, §1).

D2 (EP-A-0 042 827) is concerned with pharmaceutical compositions for topical application containing a corticosteroid as the active ingredient (p. 1, §1).

D3 (BLEEHEN S.S. et al.) compares the efficacy and safety of once-daily with twicedaily applications of a 0.05% cream formulation of fluticasone propionate in the treatment of atopic eczema in adults and children (abstract).

D4 (SPENCER C.M. et al.) discloses a review of fluticasone propionate, its pharmacological properties and therapeutic uses in the treatment of dermatological disorders (title).

Novelty

The subject-matter of claims 1, 5, 14, 18, 21 and 22 is not new in the sense of Article 33 (2) PCT.

The following claims are not new over the following documents with their cited passages:

INTERNATIONAL PRELIMINARY

D1: example 1 Claim 1: Claim 5: D1: example 1 D1: example 1 Claim 14: Claim 18: D1: example 1

example 1, p. 1, §3 and 4 D1: Claim 21: example 1, p. 1, §3 and 4 Claim 22: D1:

While D2 discloses the same auxiliary components as present claim 1 (p. 2, §3 to p. 3, §3), it is silent to the active substance fluticasone. Therefore, D2 does not anticipate novelty of present claims 1 to 24.

D3 discloses the auxiliary components as claimed in claim 1 (p. 593, left col., §4), but it is silent to the percentage of the said components. Further, it describes well the treatment of skin diseases (atopic eczema) with fluticasone (abstract; p. 592, left col. §1; p. 594, right col. §2). D3 does not anticipate novelty of present claims 1 to 24.

D4 gives an overview to the active substance fluticasone and its uses.

Inventive step

The subject-matter of claims 1 to 24 does not involve an inventive step in the sense of Article 33 (3) PCT.

For claims 1, 5, 14, 18, 21 and 22 the following applies:

Even if the applicant is able to establish novelty it cannot be seen that any particular aspect of the application as filed would involve an inventive step under Article 33 (3) PCT in the light of the relevant prior art.

For claims 2, 6, 7, 9, 12, 13, 15 to 17 the following applies:

The additional features of said claims can be determined by routine experiments and are therefore not inventive in the sense of Article 33 (3) PCT.

For claims 3 and 4 the following applies:

The additional features of claims 3 and 4 can be determined as alternatives and are therefore not inventive in the sense of Article 33 (3) PCT.



For claims 8, 10, 11, 19, 20, 23 and 24 the following applies:

The additional features of claims 8, 10, 11, 19, 20, 23 and 24 can be determined by routine experiments and are therefore not inventive in the sense of Article 33 (3) PCT.

Industrial applicability

For the assessment of the present claims 21 to 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

For the EPO the following applies:

Claims 14 and 15 are directed to the use of a medicament for the inhibition of a biological mechanism; such a use cannot be patented, since it is not considered as relating to a therapeutic application in the meaning of the decision of the Enlarged Board of Appeal Gr.05/83, O.J. 1/1983, page 64, according to which only the use of the composition of claim 1 for the manufacture of a medicament for a new and inventive therapeutic application could be patentable.



WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

51) International Patent Classification 7:		(11) International Publication Number: WO 00/24401
A61K 31/57, 7/48, 31/56	A1	(43) International Publication Date: 4 May 2000 (04.05.00
21) International Application Number: PCT/GE 22) International Filing Date: 20 October 1999 (•	Wellcome House, Berkeley Avenue, Greenford, Middlese
30) Priority Data: 9823036.0 22 October 1998 (22.10.98) 71) Applicant (for all designated States except US): GROUP LIMITED [GB/GB]; Glaxo Wellcom Berkeley Avenue, Greenford, Middlesex UB6 0N 72) Inventors; and (75) Inventors/Applicants (for US only): DOW, Ge [US/US]; Dow Pharmaceutical Science, 133 woodway, Petaluma, CA 94954 (US). JOHNSO Arthur [US/US]; Glaxo Wellcome Inc., Five Mod Research Triangle Park, NC 27709 (US). KELLY Furr [US/US]; Glaxo Wellcome Inc., Five Mod Research Triangle Park, NC 27709 (US). L Robert, William [US/US]; Dow Pharmaceutical 1330A Redwoodway, Petaluma, CA 94954 (I JAGOPALAN, Rukmini [US/US]; Glaxo Wellc Five Moore Drive, Research Triangle Park, N (US).	GLAX e Hous N (GB) ordon, OA Re N, Keit ore Driv ATHRO Science US). Ra ome Inc	ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, II KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MMD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RI SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UC, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KI LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AM AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AM BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report.
57) Abstract A fluticasone lotion having improved vasoconstrictor otion contains 0.05 weight percent fluticasone propionate	and ant	-inflammatory activity and higher than expected potency. The fluticason oil-in-water vehicle that includes excipients. The fluticasone lotion
(54) Title: FLUTICASONE LOTION HAVING IMPRO (57) Abstract A fluticasone lotion having improved vasoconstrictor otion contains 0.05 weight percent fluticasone propionate an expectedly efficacious while exhibiting an improved safe	and ant	-inflammatory activity and higher than expected potency. The fluticasor oil-in-water vehicle that includes excipients. The fluticasone lotion
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